131. Tobacco workers

Four studies were found which gave data relevant to an investigation of a possible association between lung cancer risk and tobacco work, and details of them are presented in Table 131. Standardized mortality ratios ranging from 87-147 were calculated, with three out of five being raised. Four proportional mortality ratios were also presented, and these ranged from 112-325. Lastly, one study estimated a relative risk of 15.1.

Before interpreting these results, one potential problem in the design of the study by Blair should be noted. The subjects were selected from obituary listings of the Tobacco Workers' International Union, and a failure to include workers who dropped their Union membership before death or retirement may have biased the findings.

Tobacco workers may be exposed to various chemicals during the processing of tobacco from leaf to finished product, including residues of pesticides and barn fumigants such as phosphine gas, dichlorovinyl dimethylphosphate or carbon tetrachloride, and silica and leaf dusts from processes such as stemming, tipping and redrying [1]. However, no measurements of any of these exposures were attempted by any of the studies. Workers in the study by Talcott et al were exposed to crocidolite asbestos, but no objective measurements of the level of exposure were available.

Thus, although the evidence in the table suggests that there may be an increased risk of lung cancer among tobacco workers, no clear explanation for this observation has been put forward.

Table 131: Estimates of relative risk/standardized mortality ratio for tobacco workers

Study	Population	Relative risk (95% limits)
OPCS (1978)	UK male tobacco preparers and product makers, aged 15-64	87*
	Aged 65-74	142[1]
	Married women[2] aged 65-74	325[1]
	Unmarried women aged 15-64	144*
	Aged 65-74	243[1]
Logan (1982)	UK male tobacco workers - 1951	140*
	1961	147*
	1971	87*
Blair et al (1983)	US tobacco workers	112[1]
Talcott et al (1989)	US cigarette filter factory workers	15.1(7.5-27.0)[3]

* Standardized mortality ratio

1 Proportional mortality ratio

2 According to husband's occupation

3 Incidence

References

1. Blair A, Berney BW, Heid MF and White DW (1983) Causes of death among workers in the tobacco industry. Arch Environ Health, 38, 223-228.

2. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London and IARC, Lyon.

3. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

4. Talcott JA, Thurber WA, Arlene RN et al (1989) Asbestos-associated diseases in a cohort of cigarette-filter workers. N Engl J Med, 321, 1220-1223.

132. Toluenes

Only three studies were found which attempted to investigate a possible association between lung cancer risk and exposure to toluenes, and details of these are given in Table 132. Two standardized mortality ratios, of 147 and 278, were calculated, while one study simply stated that six cases of respiratory cancer were observed.

Only the study by Walker made objective measurements of the concentrations of toluene the workers were exposed to, and none of the studies gave any information which would have allowed an estimation of the differential risk for individual toluenes. It is not really surprising then that IARC considered the evidence for the carcinogenicity of toluenes to humans to be "inadequate" [1].

Table 132: Estimates of relative risk/standardized mortality ratio for exposure to toluenes

Study	Population	Standardized mortality ratio
Sakabe et al (1976)[1]/ Sakabe and Fukuda (1977)[1]	Japanese workers	Six cases of respiratory cancer observed
Sorahan et al (1983)[1]	UK workers	278*[2]
Walker et al (1993)	US shoe factory workers	147(120-180)*

1 From International Agency for Research on Cancer (1987)

2 Estimated from data given

References

1. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 148-149. IARC, Lyon.

2. Walker JT, Bloom TF, Stern FB et al (1993) Mortality of workers employed in shoe manufacturing. Scand J Work Environ Health, 19, 89-95.

133. Tuberculosis

Table 133 details the studies which attempted to relate lung cancer risk to ever having suffered from tuberculosis. Fifty relative risks were estimated, ranging from 0.84-29.82, of which 47 were above 1.00. Two standardized proportionate mortality ratios, both of 1.50, were also estimated. In addition, one study reported a positive association between lung cancer and tuberculosis but did not provide any detailed results, another observed that lung cancer occurred 20 times more frequently in those who had suffered from tuberculosis than in the general population, and one study reported that 10.0% of male and 8.2% of female lung cancer cases had a history of tuberculosis infection. Finally, one study reported finding a correlation between lung cancer mortality in adulthood and tuberculosis mortality in the period corresponding to the childhood of the lung cancer cases.

Although many of the studies gathered information on tuberculosis infection from registers or medical records, or followed-up groups of tuberculosis patients, several studies (Alavanja, Campbell, Campbell and Hughes, Wu, Wynder, Wynder and Fairchild) appeared to based their data on information elicited at interviews with the subjects. Also, it was not clear how the data on tuberculosis infection were collected in the study by Zheng. Therefore, it is possible that these studies may contain inaccuracies due to misclassification of disease status.

The data presented in the table suggest a positive association between lung cancer risk and a history of tuberculosis infection, but on the whole the estimates of relative risk are not particularly large, and therefore the relationship does not appear to be very strong. A recent review by Aoki [2] stated that although patients with active pulmonary tuberculosis had a higher than normal risk of dying from lung cancer, there was "little biological evidence of TB lesions themselves, or TB bacilli per se, having major roles to play in the carcinogenesis of lung cancer at the moment".

Table 133: Estimates of relative risk for history of tuberculosis

Study	Population	Relative risk (95% limits)
Wynder et al (1956)[1]	Women	1.00
Campbell and Hughes (1960)[1]	Not stated	Lung cancer occurred 20 times more frequently in TB patients than in general population
Campbell (1961)[1]	Not stated	Positive association
Steinitz (1965)[3]	Israeli residents	10.0% male and 8.2% female lung cancer cases had history of TB
Wynder and Fairchild (1966)	US men	0.84(0.22-3.21)[2]
Simecek and Simeckova (1967)[3]	Czech residents	4.2
Aoki et al (1969)[3]	US white men	6.7(4.0-9.6)
	Non-white men	8.6(4.0-13.7)
	US white men, active TB	10.5
	Non-white men	20.6
	White men, inactive TB	4.5
	Non-white men	2.3
	US residents, 1962-3	3.6(1.9-5.3)
	1963-4	1.7(0.4-3.0)
	Japanese men	2.75
	Women	5.48
Aoki et al (1969)[3]/ Ipsen (1967)[3]	US men	3.1
Campbell and Guilfoyle (1970)[3]	Australian men	2.06
Kreus et al (1970)[3]	Finnish residents	2.2

Table 133 continued

Aoki and Ohtani (1971)[3]	Japanese men, 1964-68, CVD controls	1.41
	Gastric cancer controls	1.23
	Women, CVD controls	1.33
	Gastric cancer controls	1.54
	Men, 1974-82, CVD controls	4.21
	IHD controls	2.13
	Women, CVD controls	3.87
	IHD controls	2.16
Watanabe and Kurashima (1977)[3]	Japanese residents	3.56
	Japanese residents	6.93
Clemmensen and Hjalgrim-Nelson (1979)[3]	Danish men, INH+	3.36
	INH-	2.58
	Women, INH+	4.55
Howe et al (1979)[3]	Canadian men	1.50(1.21-1.47)[4]
	Women	1.50(1.11-1.98)[4]
Hongo et al (1981)[3]	Japanese men	4.88
	Women	9.69
Komatsu et al (1981)[3]	Japanese men	2.58
	Women	19.6
Mercer (1981)	English residents	Correlation between lung cancer mortality in adulthood and TB mortality in time period relating to childhood
Hinds et al (1982)	Hawaiian women	1.0(0.2-5.5)
	Japanese women	2.0(0.4-10.3)
	Chinese women	2.1(0.3-16.1)
Aoki (1985)[3]	Japanese men	12.0
	Women	5.0
Takatorige et al (1985)[3]	Japanese residents, -1 year follow-up	29.82
	1-2 years	6.36
	2-3 years	5.00
	3-4 years	4.35
	4-5 years	1.27
	5+ years	1.27

Table 133 continued

Zheng et al (1987)[3]	Chinese residents	1.5(1.2-1.8)
Wu et al (1988)	Not stated	10.0(1.1-90.1)
Sakurai et al (1989)[3]	Japanese women	6.4
Gao et al (1991)[3]	Chinese men	1.72(1.11-2.53)
	Women	2.79(1.79-4.14)
Alavanja et al (1992)	US female residents	2.0(1.0-4.1)

CVD = cardiovascular disease; IHD = ischaemic heart disease; INH = Isoniazid treatment

1 From Roe and Walters (1965)

2 Estimated from data given

3 From Aoki (1993)

4 Standardized proportionate mortality ratio

References

1. Alavanja MCR, Brownson RC, Boice JD and Hock E (1992) Preexisting lung disease and lung cancer among nonsmoking women. Am J Epidemiol, 136, 623-632.

2. Aoki K (1993) Excess incidence of lung cancer among pulmonary tuberculosis patients. Jpn J Clin Oncol, 23, 205-220.

3. Hinds MW, Cohen HI and Kolonel LN (1982) Tuberculosis and lung cancer risk in nonsmoking women. Am Rev Resp Dis, 125, 776-778.

4. Mercer AJ (1981) Risk of dying from tuberculosis or cancer: Further aspects of a possible association. Int J Epidemiol, 10, 377-380.

5. Roe FJC and Walters MA (1965) Some unsolved problems in lung cancer etiology. Progr Exp Tumor Res, 6, 126-227.

6. Wu AH, Yu MC, Thomas DC, Pike MC and Henderson BE (1988) Cancer Res, 48, 7279-7284.

7. Wynder EL and Fairchild EP (1966) The role of a history of persistent cough in the epidemiology of lung cancer. Am Rev Resp Dis, 94, 709-720.

134. Typhoid infection

Only one study could be found which attempted to relate the risk of lung cancer to typhoid, and details of it are given in Table 134. A relative risk of 2.5 was estimated.

This excess risk was only seen in chronic typhoid and paratyphoid carriers, and not in a group of people who had suffered from the acute disease but not gone on to become carriers. It was therefore suggested by the authors that an increased lung cancer risk is only associated with chronic carriers, but with only one study reporting there is no other evidence to support this view, or indeed that typhoid in any form is a risk factor for lung cancer.

Table 134: Estimates of relative risk for typhoid infection

Study	Population	Relative risk (95% limits)
Caygill et al (1994)	Scottish residents	2.5(0.82-5.89)

References

1. Caygill CPJ, Hill MJ, Braddick M and Sharp JCM (1994) Cancer mortality in chronic typhoid and paratyphoid carriers. Lancet, 343, 83-84.

135. Uranium compounds

Table 135 gives details of the studies found which provided data relevant to an investigation of the possible association between lung cancer risk and exposure to uranium compounds. Fifteen standardized mortality ratios were calculated, ranging from 82-482, with 12 being raised. One study estimated relative risks of between 0.943 and 1.027 per centigray increase in the cumulative lung dose of uranium, while two others stated that excesses of lung cancer had been observed, but failed to give any detailed results.

Various drawbacks were noted in some of the studies, which should be highlighted before an evaluation of the evidence is made. The standardized mortality ratio presented by Archer was calculated on the basis of nonwhite rates of lung cancer, and it was stated that this would have produced an overestimate of the expected number of lung cancers in the study population. It was also noted that there was a degree of overlap in the studies by Chovil, Ham and Muller, which cannot therefore be considered as completely independent of each other. Other potential problems include possible incomplete ascertainment of cases in the studies by Chovil and Kunz.

It was noted in the study by Kusiak that many of the miners were also exposed to arsenic, nickel, copper and gold, and that there was a difference in risk particularly for those miners who had also been exposed to arsenic and gold. Additionally, it is highly likely that most of the subjects in these studies were exposed to radiation, and it is possible that this is a more important factor in the observed increase in in lung cancer than the uranium itself. In fact, the National Research Council stated that "the dominant source of radiation damage to the respiratory system in miners is generally considered to be the inhalation of radon daughters, rather than the uranium content of the ore". Therefore, it is difficult to properly determine the carcinogenicity of uranium and its compounds to humans, although the evidence presented in the table is suggestive of a positive association.

Table 135: Estimates of standardized mortality ratio/relative risk for uranium compounds

Study	Population	Standardized mortality-ratio (95% limits)
Archer et al (1976)[1]	American Indian uranium miners	423(p>0.01)
Ham (1976)[1]	Canadian uranium miners	180[2]
Kunz et al (1979)[1]	Czech uranium miners	Excess lung cancer observed for all levels of cumulative exposure and exposure duration
Chovil (1981)[1]	Canadian uranium miners	Excess of lung cancer observed
Muller et al (1981, 1983,1985)[1]	Canadian uranium miners	181(p<0.05)
Waxweiler et al (1981)[1]	US white uranium miners	482(lower 95% limit 425)
Waxweiler et al (1983)[3]	US uranium workers never employed in mining	83(54-121)
Tirmarche et al (1984)[1]	French uranium miners	191[2]
Nair et al (1985)[3]	Canadian uranium miners	184
	Uranium refinery workers	82
	Surface uranium miners	175
	Underground uranium miners	375
	Other uranium workers	110
Howe et al (1986)[1]	Canadian uranium miners	190[2]
Polednak and Frome (1986)[3]	US uranium processing workers employed less than 1 year	92
	Employed 1 year or more	106
Dupree et al (1993)	US uranium processing workers	0.943-1.027[4]
Kusiak et al (1993)	Canadian uranium miners	225(191-264)

Footnote to Table 135

1 From International Agency for Research on Cancer (1988)

2 Estimated from data given

3 From National Research Council (1988)

4 Relative risk per centigray increase in cumulative lung dose

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References

1. Dupree E, Watkins J, Ingle J et al (1993) Risk of lung cancer among uranium processing workers. Am J Epidemiol, 138, 640 (Abstract).

2. International Agency for Research on Cancer (1988) Monographs on the evaluation of carcinogenic risks to humans. Volume 43: Man-made mineral fibres and radon, 173-259. IARC, Lyon.

3. Kusiak RA, Ritchie AC, Muller J and Springer J (1993) Mortality from lung cancer in Ontario uranium miners. Br J Ind Med, 50, 920-928.

4. National Research Council (1988) Health risks of radon and other internally deposited alpha-emitters: BEIR IV. National Academy Press, Washington DC.

136. Vegetarianism

Table 136 gives details of the two studies which investigated lung cancer risk in relation to a vegetarian diet. Three standardized mortality ratios, ranging from 8-89, were calculated.

While these results are indicative of a protective effect of vegetarianism, data from more studies is needed before such a relationship can be confirmed.

Table 136: Estimates of standardized mortality ratio for vegetarianism

Study	Population	Standardized mortality ratio
Kinlen (1982)	UK female members of religious orders	45
Chang-Claude and Frentzel-Beyme (1993)	German men	8
	Women	89

References

1. Chang-Claude J and Frentzel-Beyme R (1993) Dietary and lifestyle determinants of mortality among German vegetarians. Int J Epidemiol, 22, 228-236.

2. Kinlen LJ (1982) Meat and fat consumption and cancer mortality: A study of strict religious orders in Britain. Lancet, 1, 946-949.

137. Vinyl chloride

Although most of the studies which have investigated the potential effects of exposure to vinyl chloride have concentrated on liver cancer, a few studies were found which had also looked for a possible association with lung cancer, and details of these are given in Table 137. Few detailed results were available, but it can be seen from the table that of the 10 estimates of relative risk given, all but 1 were raised. Additionally, one standardized mortality ratio, of 194, was presented.

It is not clear how extensive the exposures of the subjects were, as objective measurements of vinyl chloride concentrations in the workplace do not appear to have been made by any of the studies. It is also possible that some workers may have been exposed to other chemicals which may themselves be potential carcinogens. Lastly, there are differences between the studies in the length of time a subject had to be employed for before being considered as "exposed", which may also introduce inaccuracies.

Additionally, the findings by Monson can be questioned, on the grounds that not all of the deaths studied had occurred in workers in activities directly related to vinyl chloride production or polymerization and that the study failed to include deaths among workers who had terminated employment prior to retirement or death [1].

Despite these drawbacks, IARC considered there to be "sufficient" evidence for the carcinogenicity of vinyl chloride to humans [1,2].

Table 137: Estimates of relative risk/standardized mortality ratio for exposure to vinyl chloride

Study	Population	Relative risk (95% limits)
Monson et al (1974)[1]	US vinyl chloride workers	>1.00
Tabershaw and Gaffey (1974)[1]	US vinyl chloride workers	>1.00[2]
Byren et al (1976)[1]	Swedish vinyl chloride/polyvinyl chloride workers	>1.00(p>0.05)
Fox and Collier (1976)[1]	Workers exposed to vinyl chloride for <15 years	1.56
Saric et al (1976)[1]	Yugoslavian vinyl/polyvinyl chloride workers	1.00
Waxweiller et al (1976)[1]	US vinyl chloride/polyvinyl chloride workers	194*[2]
Von Reinl et al (1977)[1]	German vinyl chloride workers	>1.00
Buffler et al (1979)[3]	Vinyl chloride workers	>1.00
Waxweiler et al (1981)[3]	Synthetic chemical plant workers	>1.00
Fedotova (1983)[3]	Vinyl chloride/polyvinyl chloride workers	>1.00
Heldaas et al (1984)[3]	Vinyl chloride/polyvinyl chloride workers	>1.00

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1979)

2 Tumours of respiratory system

3 From International Agency for Research on Cancer (1987)

References

1. International Agency for Research on Cancer (1979) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 19: Some monomers, plastics and synthetic elastomers, and acrolein, 377-438. IARC, Lyon.

2. International Agency for Research on Cancer (1979) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 373-376. IARC, Lyon.

138. Vitamin A

There has recently been much interest in the relationship between diet and the risk of cancer, and several studies have attempted to investigate the possible association between vitamin A intake and the risk of lung cancer. The results of these studies are detailed in Table 138, which also includes two overall estimates of relative risk, based on 3 and 24 studies respectively. For those studies which divided the respondents into multiple categories of vitamin A intake only the relative risk estimate for the highest, or lowest, intake category has been given, as appropriate. For the studies which used a high intake of vitamin A as the reference category, 11 out of 13 estimates of relative risk were above 1.00, ranging from 1.13-3.00. The other two studies failed to find an association, but did not report their results in detail. All of the 7 relative risks presented from the studies which compared a high intake of vitamin A to a base category of low intake were reduced, lying in the range of 0.31-0.91.

It can be seen from the table that the index of vitamin A used varied widely. A number of studies took measurements from blood samples, recording serum levels of vitamin A or beta-carotene. Most of the remaining studies concentrated on dietary intake, calculating indices of vitamin A or beta-carotene intake from the amount of certain foods eaten, although three studies simply used total consumption of vegetables, or fruits and vegetables, as an index of vitamin A intake. It is not clear how reliable indices of vitamin A intake based on dietary assessment are, especially where the frequency of consumption rather than the actual amount eaten is measured. Additionally, there may be important sources of vitamin A, such as vitamin supplements, which are not included in dietary questionnaires.

Another point to consider is the fact that vitamin A is taken into the body in two forms; as pre-formed vitamin A and as beta-carotene, from which the body is able to manufacture the vitamin as required. Therefore, it is difficult to tell whether it is the vitamin itself or the provitamin which is providing the protective effect. One further problem lies in the fact that foods are rarely a source for just one vitamin b

usually contain several. A high intake of vitamin A, therefore, could correlate with a high intake of some other component of the diet which may itself be the protective factor, rather than the vitamin.

Finally, the development of cancer may affect appetite and change the way the body metabolizes food. As a result, cancer patients may appear to have different levels of serum and dietary vitamins than those not suffering from cancer, but these could be as a result of the disease rather than a cause of it. Therefore, case-control studies of the relationship between diet and cancer should be viewed with some caution, while cohort studies, which measure vitamin levels or dietary intake before the onset of disease, may provide more reliable results.

Bearing all these potential problems in mind, the results obtained from the various studies are remarkably consistent, suggesting that there may indeed be some protective effect, although whether this is from vitamin A or beta-carotene is not clear.

Table 138: Estimates of relative risk for vitamin A intake

Study	Study type	Location	Vitamin A index	Relative risk (95% limits)
Highest intake as reference category:				
MacLennan et al (1977)	C-C	Singapore	VEG	2.23(1.49-3.33)
Hankin et al (1984)	C-C	USA	DVA	1.39(0.89-2.15)
Seigel (1984)	C-C[1]	USA/Switzerland	SVA	No association
Menkes et al (1986)	PR	USA	SVA	1.13
			SBC	2.20
Humble et al (1987)	C-C	USA	DVA	1.29(0.91-1.83)
			DBC	1.35(0.96-1.90)
Kok et al (1987)	PR	Netherlands	SVA	No association
Orentreich et al (1991)	C-C	USA	SVA	1.5
			SBC	3.0
Block et al (1992)	CO[2]	Various	FVI	2.20(1.20-7.00)
Forman et al (1992)	C-C	China	FVI	1.22(0.76-1.94)
Dorgan et al (1993)	C-C	USA	DCA	1.27(1.03-1.56)

Table 138 continued

Lowest intake as reference category:

Bjelke (1975)	PR	Norway	DVA	0.31 ($p < 0.01$)
Wald et al (1988)	PR	England	SBC	0.81(0.37-1.78)
Chow et al (1992)	PR	USA	DVA	0.80(0.50-1.20)
			DBC	0.80(0.50-1.20)
Huang et al (1992)	C-C	China	DBC	0.91(0.85-0.99)
Shibata et al (1992)	PR	USA	DBC	0.81(0.49-1.33)
Steinmetz et al (1993)	PR	USA	DBC	0.83(0.52-1.32)

C-C = Case-control; CO = Combined; DBC = Dietary beta-carotene; DCA = Dietary carotenoids; DVA= Dietary vitamin A; FVI = Fruit and vegetable intake; PR = Prospective; SBC = Serum beta-carotene; SVA = serum vitamin A; VEG = Vegetable intake;

1 Combined results from 3 studies

2 Combined results from 24 studies

References

1. Bjelke E (1975) Dietary vitamin A and human lung cancer. Int J Cancer, 15, 561-565.

2. Block G, Patterson B and Subar A (1992) Fruit, vegetables and cancer prevention: a review of the epidemiological evidence. Nutr Cancer, 18, 1-29.

3. Dorgan JF, Ziegler RG, Schoenberg JB et al (1993) Race and sex differences in associations of vegetables, fruits, and carotenoids with lung cancer risk in New Jersey (United States). Cancer Causes and Control, 4, 273-281.

4. Forman MR, Yao SX, Graubard BI et al (1992) The effect of dietary intake of fruits and vegetables on the odds ratio of lung cancer among Yunnan tin miners. Int J Epidemiol, 21, 437-441.

5. Hankin JH, Kolonel LN and Hinds MW (1984) Dietary history methods for epidemiologic studies: application in a case-control study of vitamin A and lung cancer. JNCI, 73, 1417-1421.

6. Huang C, Zhang X, Qiao Z et al (1992) A case-control study of dietary factors in patients with lung cancer. Biomed Environ Sci, 5, 257-265.

7. Humble CG, Samet JM and Skipper BE (1987) Use of quantified and frequency indices of vitamin A intake in a case-control study of lung cancer. Int J Epidemiol, 16, 341-346.

8. Kok FJ, van Duijn CM, Hofman A, Vermeeren R, de Bruijn AM and Valkenburg HA (1987) Micronutrients and the risk of lung cancer (Letter). N Engl J Med, 316, 1416.

9. MacLennan R, Da Costa J, Day NE, Law CH, Ng YK and Shanmugaratnam K (1977) Risk factors for lung cancer in Singapore Chinese, a population with high female incidence rates. Int J Cancer, 20, 854-860.

10. Menkes MS, Comstock GW, Vuilleumier JP, Helsing KJ, Rider AA and Brookmeyer R (1986) Serum beta-carotene, vitamins A and E, selenium, and the risk of lung cancer. New Engl J Med, 315, 1250-1254.

11. Orentreich N, Matias JR, Vogelman JH, Salkeld RM, Bhagavan H and Friedman GD (1991) The predictive value of serum β-carotene for subsequent development of lung cancer. Nutr Cancer, 16, 167-169.

12. Seigel D (1984) Discussion of case-control studies of Peleg, Stahelin, and Willett. JNCI, 73, 1469-1470.

13. Shibata A, Paganini-Hill A, Ross RK, Yu MC and Henderson BE (1992) Dietary β-carotene, cigarette smoking, and lung cancer in men. Cancer Causes and Control, 3, 207-214.

14. Steinmetz KA, Potter JD and Folsom AR (1993) Vegetables, fruit, and lung cancer in the Iowa Women's Health Study. Cancer Res, 53, 536-543.

139. Vitamin C

Details of some 14 studies which have attempted to investigate the possible association between vitamin C intake and the risk of lung cancer are given in Table 139, along with the key findings. Where the respondents were divided into multiple categories of vitamin C intake only the relative risk estimate for the highest, or lowest, category has been given, as appropriate. Thirteen out of the 17 estimates of relative risk presented from studies which used a high intake of vitamin C as the reference category showed a positive association, with risks ranging from 1.28-4.30, although several studies did not give details of their results. The remaining four studies failed to find an association. All of the 4 relative risks presented from the studies which compared a high intake of vitamin C to a base category of low intake were reduced, lying in the range of 0.26-0.94.

The table shows the indices of vitamin C intake used by the studies, and it can be seen that these varied widely. Only one study took measurements of serum vitamin C levels. The others measured dietary intake, calculating indices of vitamin C intake from the amount of certain foods eaten, although three studies also looked at total consumption of fruit or green salads. The reliability of nutrient indices based on dietary assessment is unclear, especially where only the frequency of consumption is measured, rather than the actual amount eaten. Additionally, as only three studies recorded usage of vitamin supplements intake of vitamin C from this source will probably not have been included by many of the studies.

One further problem lies in the fact that foods are rarely a source for just one vitamin but usually contain several. A high intake of vitamin C, therefore, could correlate with a high intake of some other component of the diet which may itself be the protective factor. In particular, foods high in vitamin C are also often high in carotenoids, for which there is some evidence of a protective effect [1]. Alternatively, a high intake of foods containing vitamin C may correlate with a low intake of foods containing nutrients, such as fat, which are believed to be positively associated with the risk of cancer.

Finally, due to the fact that the development of cancer might affect appetite and change the way the body metabolizes food, cancer patients

may appear to have different levels of serum and dietary vitamins than those not suffering from cancer, as a result of the disease rather than as a cause of it. For this reason, cohort studies which measure vitamin levels or dietary intake before the onset of disease may provide more reliable results than studies of a case-control design.

Despite these problems the results obtained are fairly consistent over the various studies, suggesting that vitamin C may indeed have a protective effect. However, due to the failure of several of the studies to present their results in detail, it is difficult to estimate the strength of such an effect if it does exist.

Table 139: Estimates of relative risk for vitamin C intake

Study	Study type	Location	Vitamin C index	Relative risk (95% limits)
Low vitamin C levels:				
Mettlin et al (1979)	C-C	USA	DVC	1.00
Shekelle et al (1981)*	PR	Not given	DVC	>1.00 (p >0.05)
Kvale et al (1983)	PR	Norway	DVC	1.00
Hinds et al (1984)	C-C	USA	DIS	1.60 (p >0.05)[1]
Kolonel et al (1985)	C-C	USA	DIS	1.28(0.69-2.38)[2]
Byers et al (1987)	C-C	USA	DVC	1.00
Kromhout (1987)*	PR	Not given	DVC	2.80 (p <0.01)
			FRU	>1.00 (p <0.05)
Stahelin et al (1987)*	PR	Not given	SVC	>1.00 (p >0.05)
Fontham et al (1988)	C-C	USA	DVC	1.50(p <0.001)
Holst et al (1988)	C-C	Netherlands	DVC	4.30
Koo (1988)	C-C	Hong Kong	FRU	2.19(1.22-5.55)
			DVC	1.96(1.15-4.76)
Le Marchand et al (1989)	C-C	USA	DIS	>1.00[1]
			DVC	>1.00[1]
			DIS	1.00[3]
			DVC	>1.00 (p >0.05)[3]

Table 139 continued

High vitamin C levels:				
Fraser et al (1991)	PR	USA	FRU	0.26(0.10-0.70)
			SAL	0.65(0.29-1.47)
Enstrom et al (1992)	PR	USA	DIS	0.94(0.52-1.71)[2]
			DVC	0.73(0.51-1.04)[2]

* Taken from Block (1991)

1 Males only

2 Estimated from data for males and females separately

3 Females only

C-C = Case-control; DIS = Dietary vitamin C, including supplements; DVC = Dietary vitamin C; FRU = Fruit intake; PR = Prospective; SAL = Green salads; SVC = Serum vitamin C

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140. Vitamin E

Details of three studies, reporting on ten populations, which attempted to relate lung cancer risk to vitamin E levels are given in Table 140. A relative risk of 1.47 was estimated by one of the studies. In addition, in five of the study groups serum vitamin E levels were lower in cases than controls, while in two groups the reverse was true. No association was reported for the other two populations.

It has been suggested that vitamin E may inhibit the formation of nitrosamines, and therefore carcinogenesis [3], but data from more studies is needed before a protective effect can be confirmed.

Table 140: Estimates of relative risk for high vitamin E intake

Study	Population	Relative risk
Fontham (1990)	Not stated	Serum vitamin E lower in cases than controls ($p<0.05$)
	Not stated	No association reported
	Hawaiians of Japanese ancestry	No association reported
Comstock et al (1992)	US residents	Serum vitamin E lower in cases than controls ($p<0.05$)
	Swiss residents	Serum vitamin E lower in cases than controls ($p<0.05$)
	US residents	Serum vitamin E lower in cases than controls ($p>0.05$)
	Finnish men	Serum vitamin E lower in cases than controls ($p>0.05$)
	Finnish women	Serum vitamin E higher in cases than controls ($p>0.05$)
	Hawaiian residents	Serum vitamin E higher in cases than controls ($p>0.05$)
Alavanja et al (1993)	US white women	1.47

References

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141. Waiters

Details of the two studies found which looked for a possible association between lung cancer risk and employment as a waiter/waitress are given in Table 141. One study gave a standardized mortality ratio of 156, while the other presented a standardized incidence ratio of 2.0.

It was suggested that the increase in lung cancer among waiters may be explained by their lifestyle, particularly their smoking and drinking habits [1]. However, with so few studies reporting it is difficult to reach any firm conclusions.

Table 141: Estimates of standardized mortality/incidence ratio for working as a waiter/waitress

Study	Population	Standardized mortality ratio
Logan (1982)	UK unmarried female waitresses, 1961	156
Kjaerheim and Andersen (1993)	Norwegian male waiters	2.0(1.3-2.9)[1]

1 Standardized incidence ratio

References

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142. Welding fumes

Table 142 gives details of the studies which investigated a possible association between lung cancer risk and exposure to welding fumes. For studies based on mortality/morbidity statistics, eight standardized mortality ratios (SMR) were given ranging from 92-151, of which seven were raised. Three proportional mortality ratios (PMR), of 100-145, were also presented, with two of these being raised. Three studies estimated relative risks (RR) which ranged from 0.85-3.5, of which two were above 1.00. Additionally, one study calculated an incidence rate of 125.8 per 100 000 per year, compared to the general male population. Eight SMRs were calculated from cohort studies and they ranged from 95-249, with seven being raised. The four RRs estimated lay in the range 1.25-4.4, while the two calculations of standardized incidence ratio were of 115 and 142. One study calculated a PMR of 104. Finally, 13 estimates of RR were made by case-control studies, and these ranged from 0.7-13.2, of which 11 were above 1.00.

Before an evaluation of the carcinogenicity of exposure to welding fumes is made, several potential drawbacks in the design of some of the studies should be pointed out. Firstly, the case-control studies suffer from the problem that although many of them investigated a long list of occupations and exposures most only reported those with which positive associations were found. Thus, the possibility of a publication bias in in favour of positive associations must be taken into account when reviewing these studies. Problems were also noted with some of the cohort studies. The study by Dunn et al/Dunn and Weir appeared to have incompletely followed up its subjects, while selection bias cannot be ruled out of the study by Becker et al, due to the inclusion of only those subjects who had undergone a technical examination.

Welding can be performed under a wide variety of industrial settings and therefore welders are potentially exposed to a great number of substances, derived from the welding process itself or from other industrial activities being performed in the immediate vicinity. Compounds which have been reported in welding fumes include chromium, nickel, fluoride, lead, aluminium, barium, and various gases and organic constituents [2]. However, as little information is available from the studies about the subjects' exposures it is not possible to separate out

the effects of any one compound. Furthermore, it was suggested that subjects in several of the studies (Becker, Dunn, McMillan and Pethybridge, Puntoni) may have been exposed to asbestos from sources other than welding, which could have biased the results [2].

Taking all this into account, it is not entirely surprising that IARC classified the evidence for the carcinogenicity of welding fumes as "limited" [2].

Table 142: Estimates of relative risk/standardized mortality ratio for exposure to welding fumes

Study	Population	Relative risk (95% limits)
Mortality/morbidity statistics:		
Guralnick (1963)[1]	US welders/flame cutters	92(64-129)*
Menck and Henderson (1976)[1]	US welders	137(101-182)*
Milham (1976)[1]	US welders/flame cutters	104(92-118)[2]
Decoufle et al (1977)[1]	US welders/flame cutters	0.85
Gottlieb (1980)[1]	US welders	3.5
Petersen and Milham (1980)[1]	US welders/flame cutters	100[2]
Logan (1982)	UK male welders - 1951	118*
	1961	122*
	1971	151*
	Married women[3] - 1961	132*
	1971	107*
Morton and Treyve (1982)[1]	US welders/burners	125.8[4]
Milne et al (1983)[1]	US welders	1.2
Gallagher and Threlfall (1983)[1]	Canadian welders	145(115-183)[2]
OPCS (1986)[1]	UK male welders	146*
Cohort studies:		
Dunn et al (1960)[1]/Dunn and Weir (1965,1968)[1]	US welders/burners	105(78-139)*
Puntoni et al (1979)[1]	Italian oxyacetylene welders	1.25(0.34-3.20)
	Electric arc welders	1.60(0.33-4.66)

Table 142 continued

Beaumont and Weiss (1980, 1981)[1]	US welders	132(98-174)*
Sjogren (1980)[5]	Swedish stainless steel welders	4.4
Polednak (1981)[1]	US welders	150(87-240)*
Fletcher and Ades (1984)[1]	UK welders	146(62-288)*
McMillan and Pethybridge (1984)[1]	UK welders	104(34-243)[2,6]
Becker et al (1985)[1]	German stainless steel welders	95(35-207)*
Newhouse et al (1985)[1]	UK welders	191*
Sjogren and Carstensen (1986)[1]	Swedish welders/gas cutters	1.3
Sjogren et al (1987)[1]	Swedish stainless-steel welders	249(80-581)*
Tola et al (1988)[1]	Finnish shipyard welders	115(76-167)[7]
	Machine shop welders	142(77-237)[7]
IARC (1989)[1]	European welders	134(110-160)*
Case-control studies:		
Breslow et al (1954)[1]	US welders/sheet metal workers doing welding	7.2(1.9-44.3)
Blot et al (1978)[1]	US welders/burners	0.7
Blot et al (1980)[1]	US welders/burners	0.9(0.4-2.3)
Buiatti et al (1985)[1]	Italian male welders	2.8(0.9-8.5)
Silverstein et al (1985)[1]	US welders/millwrights	13.2(1.1-154.9)
Gerin et al (1986)[1]	Canadian welders	2.4(1.0-5.4)
Kjuus et al (1986)[1]	Norwegian welders	1.9(0.9-3.7)
Lerchen et al (1987)[1]	US welders	3.2(1.4-7.4)
Schoenberg et al (1987)[1]	US welders/flame cutters	1.2(0.8-1.9)
Benhamou et al (1988)[1]	French welders/flame cutters	1.4(0.79-2.9)
Rinsky et al (1988)[1]	US shipyard workers with probable exposure to welding fumes	1.1(0.8-1.7)
Ronco et al (1988)[1]	Italian welders	2.9(0.87-9.8)
Keller and Howe (1993)	US construction workers	1.68(1.03-2.76)

Footnote to Table 142

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1990)

2 Proportional mortality ratio

3 According to husband's occupation

4 Incidence per 100 000 per year

5 From International Agency for Research on Cancer (1987)

6 Tumours of respiratory system

7 Standardized incidence ratio

References

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143. Wood industries

Although several studies have reported an increased risk of nasal cancer in workers in wood industries, the data concerning a possible association with lung cancer is somewhat more sparse. Details of those studies which have provided information are given in Table 143.

For workers in unspecified occupations within the wood industry two relative risks, of 1.0 and 3.3, were estimated, along with three standardized mortality ratios (SMR) ranging from 104-113, and a proportional mortality ratio (PMR) of 87.

Results were also presented according to the specific occupations of the subjects. The relative risks estimated for lumber/sawmill workers appeared to show some evidence of an increase in risk, ranging from <1.0-1.7, with two of them being above 1.00. However, the two SMRs calculated, of 33 and <80, did not.

For furniture/cabinet makers two standardized mortality ratios were given, of 96 and 110. In addition two relative risks, of 0.87 and 6.0, were presented. With so few studies reporting, it is difficult to see a clear pattern of increased or decreased risk.

Four SMRs were calculated for carpenters, ranging from 96-120, with three being raised. In addition, two PMRs, of 104 and 107 were given, along with two proportional registration ratios, of 111 and 115, and one relative risk of 0.87. These results provide limited evidence of a small increase in the risk of lung cancer among carpenters/joiners.

Lastly, the six relative risks estimated for pulp/paper workers lay in the range 1.0-2.2, with four being raised. Three SMRs were given, of between 69 and 91, along with one PMR of 100. Additionally, one study stated that the lung cancer rate was 9% higher among pulp/paper workers, although no details of the comparison population were given. It can be seen that no clear pattern of increased or decreased risk emerged.

Employees in the wood industry may be exposed to various substances, depending on the nature of their occupation and the processes it involves, which may vary from country to country. The most important exposures are wood dust, solvents and biological factors such as insects and fungal spores in untreated wood. Exhaust gases and oil mists associated with sawblade lubrication are an additional hazard for workers in sawmills, while pulp/paper workers may be exposed to numerous chemicals including gaseous sulphur compounds, chlorine and chlorine dioxide, turpentine, sodium hydroxide mist, methanol, ethanol, sulphuric

acid, furfural, hydroxymethylfurfural, cymene, acetic acid, formic acid, gluconic acid, aldonic acid and hydrogen peroxide, dusts consisting of lime, sodium sulphate, and compounds used for the control of slime and algae [1,7]. However, little information was available from the studies on the subjects' exposures, and in some of the studies there was a possibility that workers may have been employed in more than one area of the wood industry. Additionally, exposures in the various occupations within the industry are quite different, and therefore it may not be appropriate to classify workers from different occupations together, as some of the studies did.

Although IARC has classified the evidence for the association between nasal cancer and employment in furniture/cabinet-making as "sufficient", it was felt that there was not enough data available to make an evaluation of the possible association between lung cancer and employment in specific occupations within the wood industry [1].

Table 143: Estimates of relative risk/standardized mortality ratio for employment in the wood industry

Study	Population	Relative risk(95% limits)
General woodworkers:		
Harrington et al (1978)[1]	US wood/paper workers - urban	1.00
	Rural	3.3
OPCS (1978)	English/Welsh male woodworkers	113*
OPCS (1986)	UK male woodworkers, pattern makers	104*
	Married women[2]	105*
Rylander (1990)	US male mill/furniture/match/shingle/ weaver workers	87[3]
Lumber/sawmill workers:		
Milham (1974)[1]	US lumber/sawmill workers/millmen	<80*
Blot and Fraumeni (1976)[1]	US counties with lumber industries	<1.00
Harrington et al (1978)[1]	US sawmill/lumber/forestry workers	>1.0
Edling and Granstam (1980)[4]	Swedish lumberjacks	33
Blot et al (1982)[5]	US lumber/wood workers	1.7

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Table 143 continued

Furniture/cabinet makers:		
Brinton et al (1976)[1]	US furniture/fixture makers	0.87
Olsen and Sabroe (1979)[4]	Danish male carpenters/cabinet makers, aged 20-64	96(68-114)*
	Aged 65-84	110(92-127)*
Esping and Axelson (1980)[1]	Swedish furniture makers	6.0
Carpenters/joiners:		
Milham (1974)[1]	US carpenters/joiners	106.7*
Decoufle et al (1977)[1]/ Bross et al (1978)[1]	US carpenters	0.87
Harrington et al (1978)[1]	US carpenters	>1.00
OPCS (1978)	E/W male carpenters/joiners, aged 15-64	107[3]
	Aged 65-74	104[3]
	Incidence 1966-7	111($p<0.05$)[6]
	1968-9	115($p<0.01$)[6]
Olson and Sabroe (1979)[4]	Danish male carpenters/cabinet makers, aged 20-64	96(68-114)*
	Aged 65-84	110(92-127)*
Stellman and Garfinkel (1984)[4]	Male carpenters/joiners	120($p<0.05$)*
Paper workers:		
Blot and Fraumeni (1976)[1]	US southern/eastern counties with pulp/paper industries - males	Lung cancer rate 9% higher ($p<0.05$)
Menck and Henderson (1976)[1]	US paper manufacturing/sales workers	1.71($p<0.01$)
Blot et al (1978)[1]	US paper mill workers	1.0
Gottlieb et al (1979)[1]	US paper industry workers	1.05(0.79-1.40)
Logan (1982)	UK male paper makers - 1951	69*
	1961	84*
	1971	91*
Milham and Demers (1974)[4]	US pulp/paper workers	100[3]
Nurminen and Hernberg (1984)[4]	Pulp/paper workers	2.2(0.7-6.7)

Table 143 continued

Robinson et al (1986)[4]	US pulp/paper workers	1.00
Toren et al (1991)	Swedish paper mill workers	1.1(0.3-1.3)

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1981)

2 According to husband's occupation

3 Proportional mortality ratio

4 From International Agency for Research on Cancer (1987)

5 From Williams Pickle (1984)

6 Proportional registration ratio

References

1. International Agency for Research on Cancer (1981) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 25: Wood, leather and some associated industries, 99-138. IARC, Lyon.

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